MicroRNA-218: A Novel Therapeutic Agent for Motoneuron Diseases and Use of Its Promoter for Targeted Gene Therapy

INVENTION: Investigators at the Salk Institute have demonstrated that microRNA-218 (miR-218) is abundantly and selectively expressed by developing and mature motoneurons. The use of the mir-218 promoter allows for extremely specific gene activation in motor neurons of all known types, including spinal and cranial. Loss of miR-218 in mice was also shown to result in defects characteristic of motoneuron diseases such as amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy (SMA). This work has implications for the use of microRNA-218 as a targeted treatment of motoneuron diseases.

APPLICATIONS:

- Use of mir-218 promoter sequence provides a highly specific means to target expression to motoneurons
- Use of mir-218 itself as a potential therapeutic intervention for motoneuron diseases

ADVANTAGES:

- Previous promoters used for motoneuron expression have shown off-target expression and large in size, hindering their use in gene therapy approaches. The mir-218 promoter sequence provides a highly specific means to target and is small enough to be useful for gene therapy applications.

STAGE OF DEVELOPMENT:

- Testing in mouse models for motoneuron disease
- Studying expression of miR-218 in clinical samples for validation

BACKGROUND: Motoneurons are nerve cells that are specialized such that they communicate with other cell types, including muscles and glands. Motoneurons carry signals from the brain to these other cell types and from these cells back to the brain, resulting in essential life processes for the organism, including humans.
Motoneuron dysfunction and degeneration is implicated in a number of debilitating diseases such as ALS, primary lateral sclerosis, progressive muscular atrophy, SMA, progressive bulbar palsy and pseudobulbar palsy. These diseases are characterized by deterioration in actions reliant on voluntary muscle activity such as speaking, walking, breathing, and swallowing, causing increasing disability and, eventually, death.
Therapeutic research into motoneuron disease has focused on three broad avenues: drugs, gene therapy, and the use of stem cells. As yet, there is no cure or standard treatment for motoneuron diseases and, in the absence of disease-modifying treatment, most are managed through symptomatic and supportive care focused on maintaining quality of life.

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PATENT STATUS: PCT application WO 2016/191048 pending

PUBLICATIONS: Amin, et al. (2015) Loss of motoneuron-specific microRNA-218 causes systemic neuromuscular failure. *Science, 350:1525-9.*
http://www.salk.edu/news-release/loss-of-tiny-genetic-molecules-could-play-role-in-neurodegenerative-diseases/

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TECHNOLOGY ID: S2014-102